

We claim:

1. A method of synthesizing nucleic acid molecules with reduced levels of cross hybridization, wherein at least one of the molecules synthesized is characterized by an ability to hybridize to at least one other nucleic acid molecule, comprising steps of:

- a) providing at least one nucleic acid template;
- b) providing nucleotide precursors sufficient to synthesize a nucleic acid molecule using the nucleic acid template, wherein said precursors include at least one pair of complementary precursors characterized by a reduced ability to form base pairs with each other, and further characterized by an ability to form at least one base pair with another nucleotide; and
- c) contacting the template and nucleotide precursors with an enzyme characterized by an ability to polymerize the precursors under conditions and for a time sufficient for synthesis of the nucleic acid molecule.

2. The method of claim 1, wherein the step of providing a template, the template is RNA, messenger RNA, DNA, genomic DNA, plasmid DNA or DNA reverse transcribed from RNA.

3. The method of claim 1, wherein the step of providing nucleotide precursors, the precursors contain A' and T' wherein A' and T' have a reduced ability to form a stable hydrogen-bonded base pair, wherein A' can form a stable base pair with T* and wherein T' can form a stable base pair with A*.

4. The method of claim 3, wherein A' is 2-aminoadenosine triphosphate, T' is 2-thiothymidine triphosphate, A* is adenine and T* is thymidine.

5. The method of claim 1, wherein the step of providing nucleotide precursors, the precursors contain G' and C' wherein G' and C' have a reduced ability to form a stable

hydrogen-bonded base pair, wherein G' can form a stable base pair with C*, and wherein C' can form a stable base pair with G*.

6. The method of claim 5, wherein G' is inosine triphosphate, C' is pyrrolo-pyrimidine triphosphate, G* is guanosine and C* is cytidine.

7. The method of claim 5, wherein G' is guanosine triphosphate, C' is 2-thioC triphosphate, G* is inosine triphosphate and C* is cytidine triphosphate.

8. The method of claim 1, wherein the step of providing nucleotide precursors, the precursors are selected from the group consisting of: 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine 5'-triphosphate, deoxyinosine 5'-triphosphate, deoxypyrrolopyrimidine 5'-triphosphate, 2-thiodeoxycytidine 5'-triphosphate, deoxyguanosine 5'-triphosphate, deoxycytidine 5'-triphosphate, deoxyadenosine 5'-triphosphate, deoxythymidine 5'-triphosphate, and combinations thereof.

9. The method of claim 1, wherein the step of contacting, the enzyme is selected from the group consisting of: RNA polymerase, DNA polymerase, reverse transcriptase, ribozyme, and self-replicating RNA molecule.

10. The method of claim 1, wherein the nucleic acid molecules with reduced levels of cross hybridization are used in a ligase assay, a polymerase extension assay, or a nucleic acid array assay.

11. The method of claim 1, wherein the step of providing nucleotide precursors comprises providing at least one nucleotide precursors having a purine analog and at least one nucleotide having a pyrimidine analog wherein the purine analog and the pyrimidine analog are not capable of forming a stable hydrogen bonded base pair, and wherein at least one of

the purine or pyrimidine analogs is capable of forming a stable hydrogen bonded base pair with another complementary analog or complementary natural base.

12. A method of producing nucleic acid molecules with a reduced levels of cross hybridization, wherein at least one of the molecules is characterized by an ability to hybridize to at least one other nucleic acid molecule, comprising steps of:

- a) providing a first nucleic acid template having a first sequence element;
- b) providing a second nucleic acid template having a second sequence element, wherein the second sequence element is substantially complementary to the first sequence element;
- c) providing nucleotide precursors sufficient to synthesize a first nucleic acid molecule using the first nucleic acid template and a second nucleic acid molecule using the second nucleic acid template, wherein said precursors include pairs of complementary precursors characterized by a reduced ability to form base pairs with each other, and further characterized by an ability to form at least one base pair with another nucleotide;
- d) contacting the first template and nucleotide precursors with an enzyme characterized by an ability to polymerize the precursors under conditions and for a time sufficient for synthesis of the first nucleic acid molecule; and
- e) contacting the second template and nucleotide precursors with an enzyme characterized by an ability to polymerize the precursors under conditions and for a time sufficient for synthesis of the second nucleic acid molecule, wherein at least one of the nucleic acid molecules synthesized is characterized by an ability to hybridize to a third nucleic acid molecule.

13. The method of claim 12, wherein the step of contacting the first template and nucleotide precursors and the step of contacting the second template and nucleotide precursors are performed simultaneously in one reaction.

14. The method of claim 12, wherein the step of providing a first template and wherein the step of providing a second template, the templates are selected from the group consisting of: RNA, messenger RNA, DNA, genomic DNA, plasmid DNA or DNA reverse transcribed from RNA.

15. The method of claim 12, wherein the step of providing nucleotide precursors, the precursors contain A' and T' wherein A' and T' have a reduced ability to form a stable hydrogen-bonded base pair with each other, wherein A' can form a stable base pair with T* and wherein T' can form a stable base pair with A*.

16. The method of claim 15, wherein A' is 2-aminoadenosine triphosphate, T' is 2-thiothymidine triphosphate, A* is adenosine and T* is thymidine.

17. The method of claim 12, wherein the step of providing nucleotide precursors, the precursors contain G' and C' wherein G' and C' have a reduced ability to form a stable hydrogen-bonded base pair, wherein G' can form a stable base pair with C*, and wherein C' can form a stable base pair with G*.

18. The method of claim 17, wherein G' is inosine triphosphate, C' is pyrrolo-pyrimidine triphosphate, G* is guanosine and C* is cytidine.

19. The method of claim 17, wherein G' is guanosine triphosphate, C' is 2-thioC triphosphate, G* is inosine and C* is cytidine.

20. The method of claim 12, wherein the step of providing nucleotide precursors, the precursors are selected from the group consisting of: 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine 5'-triphosphate, deoxyinosine 5'-triphosphate, deoxypyrrolopyrimidine 5'-triphosphate, 2-thiodeoxycytidine 5'-triphosphate, deoxyguanosine 5'-triphosphate,

deoxycytidine 5'-triphosphate, deoxyadenosine 5'-triphosphate, deoxythymidine 5'-triphosphate, and combinations thereof.

21. The method of claim 12, wherein the step of contacting, the enzyme is selected from the group consisting of: RNA polymerase, DNA polymerase, reverse transcriptase, ribozyme, and self-replicating RNA molecule.

22. The method of claim 12, wherein the nucleic acid molecules are used in a ligase assay, a polymerase extension assay, or a nucleic acid array assay.

23. The method of claim 12, wherein the step of providing nucleotide precursors comprises providing at least one nucleotide precursors having a purine analog and at least one nucleotide having a pyrimidine analog wherein said purine analog and said pyrimidine analog are not capable of forming a stable hydrogen bonded base pair, and wherein at least one of the purine or pyrimidine analogs is capable of forming a stable hydrogen bonded base pair with another complementary analog or complementary natural base.

24. A kit comprising nucleotide precursors including pairs of complementary precursors characterized by a reduced ability to form base pairs with each other, and further characterized by an ability to form at least one base pair with another nucleotide, the kit further comprising at least one enzyme capable of polymerizing the precursors into a polynucleotide molecule, and comprising reaction buffers.

25. The kit of claim 24 comprising an enzyme capable of polymerizing nucleotide precursors into a polynucleotide molecule, buffer solutions, and nucleotide precursors selected from the group consisting of: 2-aminodeoxyadenosine 5'-triphosphate, 2-thiodeoxythymidine 5'-triphosphate, deoxyinosine 5'-triphosphate, deoxypyrrrolopyrimidine 5'-triphosphate, 2-thiodeoxycytidine 5'-triphosphate, deoxyguanosine 5'-triphosphate, deoxycytidine 5'-triphosphate, deoxyadenosine 5'-triphosphate, deoxythymidine 5'-

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triphosphate.

26. The kit of claim 24, wherein the enzyme is selected from the group consisting of:
RNA polymerase, DNA polymerase, reverse transcriptase, ribozyme, and self-replicating
RNA molecule.

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